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Poster Sessions

Protective effects of nicotinic acetylcholine receptor ligands via different mechanisms against inflammatory microglia-induced dopaminergic neuronal death.

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Inflammatory microglial activation is implicated in progressive dopaminergic neuronal loss of Parkinson's disease. Although $\alpha 7$ nicotinic acetylcholine receptors (nAChRs) have been reported to be expressed in microglia, the function of them is unclear. Here, we investigated the effect of nicotine or PNU-120596 (PNU), a positive allosteric modulator of $\alpha 7$ nAChRs on dopaminergic neuronal death induced by microglial activation. Both nicotine and PNU inhibited LPS/IFN γ -induced dopaminergic neuronal death in primary mesencephalic cultures. PNU suppressed nitric oxide release induced by LPS/IFN γ , whereas nicotine had no effect. Methyllaconitine, an $\alpha 7$ nAChR antagonist, canceled the nicotine-induced neuroprotection, but did not affect PNU-induced suppression of nitric oxide release. Nicotine induced the phosphorylation of Akt. LY294002, an inhibitor of PI3K, suppressed the neuroprotective effect elicited by nicotine. On the other hand, PNU inhibited the phosphorylation of JAK2 and STAT1 induced by IFN γ in primary microglia. These results suggest that nicotine and PNU suppress dopaminergic neuronal death mediated by microglial activation through the different mechanisms.